NEWS RELEASE

New Evidence Published Supporting Use of DecisionDx®-SCC Test in Guiding and Improving Treatment Pathway Decisions in NCCN High-Risk Cutaneous Squamous Cell Carcinoma

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New validation study shows DecisionDx-SCC significantly outperforms current staging systems in predicting risk of local recurrence and metastasis for NCCN high-risk patients

Clinician survey confirms test results align with treatment decision-making thresholds for adjuvant radiation therapy and surveillance imaging

FRIENDSWOOD, Texas, Aug. 25, 2025 (GLOBE NEWSWIRE) -- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, today announced the publication of two new studies related to its DecisionDx-SCC test, adding to its validated uses for patients with high-risk cutaneous squamous cell carcinoma (SCC).[1,2] DecisionDx-SCC is a gene expression profile test (40-GEP) designed to use a patient's tumor biology to predict individual risk of metastasis as well as response to adjuvant radiation therapy (ART).

The **first study** represents an expanded clinical use milestone, demonstrating that DecisionDx-SCC predicts local recurrence in patients classified as high-risk by National Comprehensive Cancer Network (NCCN) guidelines who have undergone Mohs resection, thereby adding a third use to the test's existing capabilities.[1] The test has now been shown to predict individual risk of metastasis, response to ART and individual risk of local recurrence, providing comprehensive results to support tailored post-surgical management and treatment pathway recommendations for patients with SCC. The **second study** shares results from a clinician survey, affirming the

impact of the test's results in guiding these recommendations, specifically the use of ART and surveillance imaging, by providing actionable decision points based on individual patient risk.[2]

"These new data indicate that DecisionDx-SCC test results provide individualized risk predictions that doctors can use to guide risk-aligned escalation or de-escalation of care in their NCCN high-risk SCC patients," said Désirée Ratner, M.D., Mohs micrographic surgeon and clinical professor of dermatology at the NYU Grossman School of Medicine in New York. "The ability of the test to reliably identify those patients with NCCN high-risk SCC at risk of developing local recurrence or metastasis is not only practice-changing for physicians who treat SCC, but also life-changing for their patients."

While most patients with NCCN high-risk SCC can be treated successfully with Mohs surgery, a subset of these patients will experience local recurrence and/or metastasis. Current staging systems, including American Joint Committee on Cancer (AJCC) version 8 staging and Brigham and Women's Hospital (BWH) T-staging, inadequately identify which patients are at highest risk for poor outcomes, creating a critical clinical need for better risk stratification tools. This limitation makes it challenging for clinicians to determine optimal treatment strategies, leading to over-treatment of low-risk patients and under-treatment of high-risk patients who may benefit from escalated approaches such as ART or enhanced post-surgical surveillance. These two new studies contribute to growing evidence that DecisionDx-SCC has the potential to address this clinical gap by enabling risk-aligned treatment decisions based on a patient's individual tumor biology rather than population-based staging criteria alone.

Key highlights of the studies include the following:

- Among 414 NCCN high-risk SCC patients with negative margins following Mohs surgery, DecisionDx-SCC significantly stratified both local recurrence and metastatic risk. Three-year survival rates decreased progressively across risk classes: local recurrence-free survival (LRFS) was 95.3% (Class 1, low risk) vs. 85.5% (Class 2A, higher risk) vs. 71.4% (Class 2B, highest risk), P=0.001; metastasis-free survival (MFS) was 97.1% vs. 89.3% vs. 57.1%, P<0.001.
- In contrast, BWH and AJCC staging systems failed to significantly stratify LRFS (log-rank, P=0.6) and MFS (log-rank, P=0.8).[1]
- DecisionDx-SCC test results (Class 2A and 2B), immunosuppression and perineural invasion were significant predictors of local recurrence, with hazard ratios of 2.6, 5.3, 2.3 and 3.7, respectively (all P<0.05). When combined with these two clinicopathologic factors which have a well-established association to a high risk of metastasis, DecisionDx-SCC demonstrated significant improvement in predictive accuracy compared to the clinicopathologic factors alone (likelihood ratio: 21.65 vs. 12.27).[1]
- The 244 clinicians surveyed in the second study most often recommended ART for patients with ≥20% risk of

local recurrence or metastasis, and surveillance imaging for patients with ≥10% risk of metastasis.[2]

- Accordingly, DecisionDx-SCC Class 2A results accurately predicted risk above the 10% threshold where most clinicians would recommend surveillance imaging and consider ART, while Class 2B results predicted risk above the 20% threshold where most clinicians would recommend proceeding with ART.[1,2]
- Clinicians who use DecisionDx-SCC reported a Class 2B test result to be among the most important risk factors they consider when making management decisions for ART.[2]

Together, these studies provide compelling support for the use of DecisionDx-SCC in clinical practice to precisely identify NCCN high-risk patients above and below established risk thresholds, enabling clinicians to better align treatment strategies with individual patient risk and potentially improving outcomes within established NCCN treatment pathways.

About DecisionDx-SCC

DecisionDx-SCC is a 40-gene expression profile test that uses an individual patient's tumor biology to predict individual risk of cutaneous squamous cell carcinoma metastasis for patients with one or more risk factors. The test result, in which patients are stratified into a Class 1 (low), Class 2A (higher) or Class 2B (highest) risk category, predicts individual metastatic risk to inform risk-appropriate management. Peer-reviewed publications have demonstrated that DecisionDx-SCC is an independent predictor of metastatic risk and that integrating DecisionDx-SCC with current prognostic methods can add positive predictive value to clinician decisions regarding staging and management. Learn more at **www.CastleBiosciences.com**.

About Castle Biosciences

Castle Biosciences (Nasdaq: CSTL) is a leading diagnostics company improving health through innovative tests that guide patient care. The Company aims to transform disease management by keeping people first: patients, clinicians, employees and investors.

Castle's current portfolio consists of tests for skin cancers, Barrett's esophagus and uveal melanoma. Additionally, the Company has active research and development programs for tests in these and other diseases with high clinical need, including its test in development to help guide systemic therapy selection for patients with moderate-to-severe atopic dermatitis seeking biologic treatment. To learn more, please visit **www.CastleBiosciences.com** and connect with us on **LinkedIn**, **Facebook**, **X** and **Instagram**.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of

1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, which are subject to the "safe harbor" created by those sections. These forward-looking statements include, but are not limited to, statements concerning: the ability of DecisionDx-SCC to support improved, risk-aligned treatment pathway decisions; the significant prognostic capabilities of DecisionDx-SCC and its ability to (i) enhance risk stratification beyond traditional staging and (ii) equip clinicians with actionable results to enable more precise, personalized treatment decisions and optimize patient management and care. The words "believe," "can" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements that we make. These forward-looking statements involve risks and uncertainties that could cause our actual results to differ materially from those in the forward-looking statements, including, without limitation: subsequent study or trial results and findings may contradict earlier study or trial results and findings or may not support the results obtained in these studies, including with respect to the discussion of our tests in this press release; actual application of our tests may not provide the aforementioned benefits to patients; and the risks set forth under the heading "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2024, and our Quarterly Report on Form 10-Q for the quarter ended June 30, 2025, each as filed with the SEC, and in our other filings with the SEC. The forward-looking statements are applicable only as of the date on which they are made, and we do not assume any obligation to update any forward-looking statements, except as may be required by law.

1. Ratner D, Arron ST, Kim YJ, et al. The 40-Gene Expression Profile Test Identifies Patients with National Comprehensive Cancer Network High-Risk Cutaneous Squamous Cell Carcinoma at High Risk of Poor Outcomes to Inform Management Decisions. J of Skin. 2025;9(4):2426-2443. doi:10.25251/mvr2rn83
2. Shah M, Zakria D, Rogers JH, et al. Actionable Risk Thresholds for Adjuvant Radiation Therapy and Surveillance Imaging in High-Risk Cutaneous Squamous Cell Carcinoma. J of Skin. 2025;9(4):2444-2461. doi:10.25251/83v2hr07

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